DRAWINGS

Applicants acknowledge with appreciation the deferment of the requirement for drawing correction pending allowance of this application.

REJECTION UNDER 35 U.S.C. §112, FIRST PARAGRAPH

The premising of this rejection upon 35 U.S.C. §112, first paragraph, was not previously understood. Since the Examiner and Applicants' counsel are in agreement that the disclosure of copending, commonly assigned Application Serial. No. 09/139,720 *is incorporated* herein by reference, it was (and still is) hard to see how it could be said that the *disclosure* is "nonenabling".

Applicant's attorney greatly appreciates the Examiner's careful and detailed explanation in the present Office Action's discussion of this rejection of the need to claim specifically the steps and procedures set forth in Application Serial No. 09/139,720 and incorporated herein by reference that are needed to produce the antibodies used in the assay of this invention. In the claims presently submitted, a conscientious effort has been made to do exactly that. It is accordingly believed that the present claims *do* overcome this rejection.

REJECTION BASED ON 35 U.S.C. §112, SECOND PARAGRAPH

Claims 10-35 have been carefully drawn in an effort to overcome this rejection. In particular independent Claims 10 and 25 now each recite a series of steps showing how the enzyme immunoassay is performed. These steps include, *inter alia*, a step of contacting the

sample suspected of containing the antigen of interest with enzyme-labelled antibody and a detection step, as well as a step for correlating detection of the antigen with concentration of the suspected *Legionella* bacteria in the water sample.

These claims are not, and should not, however, be limited to *Legionella pneumophila* detection. Other species of *Legionella* may be assayed for in the manner covered by each of the independent claims, as this application and its antecedent, Serial No. 09/139,720 which is incorporated by reference, both teach.

It is believed that the claims as now presented comply with the Office Action's requirement in numbered paragraph 6, for positive recitation of specific steps.

REJECTIONS
BASED ON 35 U.S.C. §103

It is not obvious from any combination of the references cited by the Examiner that an assay for concentration of a target *Legionella* bacterium in environmental water, which assay has the specificity and sensitivity disclosed by Applicants, could ever be achieved by the combining the cited references in the manner suggested by the Examiner. Nor is it correct, as the Examiner suggests, that mere routine manipulation of amounts of water in the sample or of antibody in the test accounts for the specificity and sensitivity that Applicants' assay achieves.

In addressing the rejection as made, Applicants recognize that it is directed to the now cancelled claims 1-9 and that new claims 10-35 are specific in ways that necessarily overcome some of the Examiner's premises for making that rejection. In particular, the rejection is based upon a *fiction*, that the monoclonal antibodies disclosed by Strosberg *et al* are somehow

the same as Applicants' antigen-specific antibodies obtained by purifying polyclonal antibodies by passing them over the highly purified O-carbohydrate antigen of the same species or serogroup of a species of *Legionella* (linked to a chromatographic column) as the purified antibodies are thereafter used to detect. Applicants do not contend that their purified antibodies are monoclonal. Rather Applicants teach *only* that their purified antibodies have high specificity for the *raw* O-carbohydrate antigen corresponding to the purified one present on the affinity column. Moreover, the statement in the action that "Strosberg *et al* teaches monoclonal antibodies to *Legionella pneumophila* purified by an affinity column to be used to detect bacteria in environmental water "(par. 8 of the action, p.6) is *wrong*. The only reference to "affinity chromatography" found in the Strosberg *et al* reference appears at col. 4 lines 27-28, in connection with making the Strosberg *et al* monoclonal antibodies useful as therapeutic agents, to be administered intravenously, against bacteremia. There is *no* indication that the Strosberg ever so treated the monoclonal antibody preparation of Example 5 (Col. 9, line 27-65).

Moreover, the monoclonal antibody discussed never was sufficiently useful in an assay for practical use to justify the assignee of the patent, Institute Pasteur, in paying even so much as the *first* maintenance fee on it. Institut Pasteur is affiliated with one or more companies that would have licensed the patent and sold, e.g., immunological diagnostic kits, as postulated in col. 4, lines 56-66 of the patent , if these monoclonal antibodies had been proved, in further testing, to have any real promise in *a Legionella* diagnostic or environmental test. Since records of the PTO conclusively show that this patent was *abandoned* on October 25, 1992, it must be presumed they did not.

By contrast, the anti-*Legionella* antibodies employed in the presently claimed assay of environmental water have proved to be extremely efficacious.

Applicants' assignee, Binax, Inc. has received FDA approval for the rapid (15-minute) ICT test for *Legionella pneumophila* serogroup 1 that shows high specificity and sensitivity for, and has greatly facilitated the diagnosis of disease caused by that bacterium in human patients. Applicants found, however that successful testing of environmental water samples required an even more sensitive and specific test (as the disclosure of the present application in fact recounts) and accordingly developed the test covered by claims 10-35 for this specific purpose. This environmental assay was made available for sale to those in need of testing environmental water shortly after the December 1999 filing for this application and has been found to be extremely helpful in the effort to identify and correct environmental water problems before they cause widespread human disease, as well as in monitoring environmental water to ensure that it is not a possible source of serious respiratory disease in humans who utilize the water for drinking, bathing, cooking, etc.

It is noted that the overall processes (a) disclosed in Serial No. 09/139,720 and incorporated herein by reference and (b) specifically disclosed herein are applicable to other *Legionella* bacteria and that the reason why both the ICT-based human diagnostic test and the enzymeimmunoassay for environmental water have initially been commercialized for *Legionella pneumophila* serogroup 1 is that this species serogroup has long been recognized in the art as causative of about 80% of the *Legionella*--caused human disease. Moreover, while there have been many efforts by many groups to develop efficacious and relatively rapid tests for detecting *Legionella* bacteria, only two--the Binax ICT test and an EIA test for *Legionella*

pneumophila serogroup 1--have ever received FDA approval for use in human patient diagnosis.

The rejection as articulated in the Office Action combines Strosberg *et al* with Imrich *et al*, Cuatrecasas *et al*, and, as to certain of the prior claims, Yen *et al*. On behalf of Applicants, it is pointed out that :

(1) the Strosberg *et al* reference is directed to the use of a very different antibody which is a monoclonal antibody, over which the use of Applicants' *different* purified polyclonal antibody should be patentable as representing a different way of identifying *Legionella* species in environmental water;

(2) there is *no* suggestion or direction in any of the combined group of references that they should be combined, or that one of ordinary skill in the art seeking antibodies of high specificity and sensitivity to identify *Legionella* bacteria would somehow be motivated to seek out and combine them in order to devise a way to improve the performance of raw polyclonal antibodies in detecting a *Legionella* species or serogroup of a species;

(3) Applicants do not contend they have invented enzyme immunoassay methods generally, or labels for use in such assays, or affinity chromatography or the use of spacer molecules to bind antigens to chromatographic columns; rather, what applicants contend is that they have invented an integral process which results in very sensitive and specific purified polyclonal antibodies against *Legionella* species and serogroups of species which, when then used in particular assays, produce outstandingly useful results--results which (a) could not have been anticipated until

arrived at by them and (b) certainly could not have been discerned in advance from reading the combined references.

The Examiner's addition of the Yen *et al* reference to reject former Claim 4 is not understood. The present application contemplates the use of magnetic microspheres, if at all, only in a preliminary step to the assay which concentrates the bacteria present in a water sample of at least 100 ml. Applicants do not contemplate the use of such microspheres as labels in the subsequent assay procedure. Moreover, applicants do not contend they invented this pre-assay concentration step *per se*, but only its combination with other steps in an integral process as set forth in claim 25.

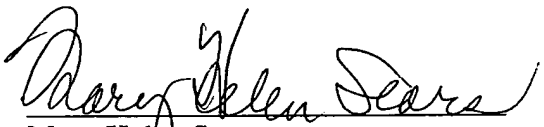
Still further, the Jürgens *et al* article cited in the office action does not, when combined with the other references cited, render any integral procedure within the scope of Applicant's present claims obvious to any person of *ordinary skill* in immunology. It certainly gives no suggestion of how to arrive at an efficacious assay for detecting any *Legionella* species or serogroup thereof in environmental water--and like each of the other references cited provides no clue that it should be combined with any of the others for any purpose.

The cited references should be withdrawn because they do not, in combination, make out an obviousness case against the present claims under 35 U.S.C. §103 as that statute has been interpreted by the Court of Appeals for the Federal Circuit.

CONCLUSION

The present claims 10-35 are, it is believed, in condition for allowance and early action to that effect is courteously requested.

Respectfully submitted,



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